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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/658,529

09/10/2003

Cary James Miller

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KATTEN MUCHIN ROSENMAN LLP  
(C/O PATENT ADMINISTRATOR)  
2900 K STREET NW, SUITE 200  
WASHINGTON, DC 20007-5118

EXAMINER

YU, MELANIE J

ART UNIT

PAPER NUMBER

1641

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/658,529	<b>Applicant(s)</b> MILLER ET AL.	
	<b>Examiner</b> MELANIE YU	<b>Art Unit</b> 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 13 February 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,2,5-7,9-12 and 69-71 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,5-7,9-12 and 69-71 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 November 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/19 and 2/2</u> .   | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

1. Applicant's amendment filed 13 February 2009 has been entered. Replacement drawings for Figures 1-21 have also been entered.

### ***Status of the Claims***

2. Claims 1, 2, 5-7, 9-12 and 69-71 are currently pending in this application and are examined on the merits.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
  2. Ascertaining the differences between the prior art and the claims at issue.
  3. Resolving the level of ordinary skill in the pertinent art.
  4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
3. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang (US 6,670,115) in view of Litman et al. (US 5,156,953).

Zhang teaches an immunosensor system, comprising: a first immunosensor that includes a first immobilized antibody and generates a first signal (detection working electrode having an immobilized specific binding capture ligand, col. 3, lines 36-55; first

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signal is generated by a current produced by applying a potential between working and reference electrodes, col. 20, lines 33-39) based on a sandwich between the first immobilized antibody, a target analyte and a labeled antibody (analyte is bound to the substrate through the first immobilized antibody, col. 3, lines 46-55 and label is attached to analyte, col. 4, lines 43-52), wherein a portion of the signal arises from non-specific binding of the labeled antibody (although small, at least a portion of the first signal is due to non-specific binding, col. 28, line 40-col. 29, line 6); a second immunosensor (auxiliary electrode bound to the same substrate as the working electrode, col. 15, lines 3-6; auxiliary electrode, Fig. 7A) that generates a second signal that is compared to the first signal (potential applied between working electrode and auxiliary electrode to generate a second current signal that is compared to the potential applied between the working and reference electrodes that generates a first current signal, col. 20, lines 33-39 and col. 20, lines 27-44); and an analyzer configured to determine a corrected signal from the first and second signals (presence of analyte is determined by correlating the first and second signals, col. 18, line 35-col. 19, line 4). Zhang et al. fail to teach the second (auxiliary) electrode being a second immunosensor that includes a second immobilized antibody and acts as an immuno-reference sensor that generates a second signal that is predictably related to the degree of non-specific binding on the first immunosensor and also fail to specifically teach the immunoreactive compound being an endogenous or exogenous protein.

Litman et al. teach a system comprising:

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a first immunosensor that generates a first signal based on a sandwich between a first immobilized antibody, a target analyte and a labeled antibody wherein a portion of the first signal arises from non-specific binding of the labeled antibody (measurement surface has sandwich assay where analyte serves as the bridge between an immobilized binding member and a labeled binding member, col. 9, lines 3-10), and

a second immunosensor (calibration surface, col. 6, lines 43-49) that includes a predetermined amount of second immobilized antibody (antibody receptor immobilized on calibration surface, col. 12, lines 22-25; present in predetermined amount, col. 14, line 68-col. 15, line 3), acts as an immuno-reference sensor, generates a second signal that is related to the degree of non-specific binding (signal from calibration surface is measured and when a quantitative determination is made by dividing the measurement signal by the calibration signal, non-specific effect are divided out and therefore the amount of second signal generated by the calibration surface is related to the amount of non-specific binding, col. 12, lines 8-17), and has an immunocomplex between the second immobilized antibody an exogenous protein that is in the sample and not the target analyte (antibody immobilized on the antibody binds to an anti(antibody), col. 12, lines 22-25, wherein the anti(antibody), calibration ligand, is labeled, col. 14, lines 12-15, and is in the sample solution because the measurement and calibration surfaces are contacted simultaneously with the same sample, col. 7, line 65-col. 8, line 3, therefore the added labeled anti(antibody) is an exogenous protein in the sample), in order to provide a qualitative analysis of whether an analyte is present in a sample above or below a predetermined amount.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include on the second immunosensor of Zhang et al., a predetermined amount of a second immobilized antibody that binds to an exogenous protein in the sample that is not the target analyte as taught by Litman et al., in order to provide an accurate detection assay technique that divides out non-specific binding effects.

With respect to claim 2, Zhang teaches the first and second immunosensor being electrochemical sensors (col. 4, line 66-col. 5, line 22).

Regarding claim 5, Zhang teaches the first and second immunosensor in a disposable cartridge (Fig. 8A-8B; col. 5, line 65 and col. 4, line 66-col. 5, line 12).

With respect to claim 6, Zhang teaches the target analyte being Troponin I (col. 13, lines 47-53 and col. 5, line 59-col. 6, line 4).

With respect to claims 9 and 12, the claims are drawn to the properties of a sample to be tested in the immunosensor system, the concentration of endogenous or exogenous protein in a sample and the type of sample. While the prior art does not specifically recite the concentration of protein in the sample as claimed, such a limitation is merely an intended use which the prior art would inherently be capable of doing. The only distinction between applicant's claims and the prior art is recited in the functional language. It is incumbent upon applicant to show that the application disclosed by Zhang is not actually capable of performing such functions. See *In re Ludtke* 1971, 169 USPQ 563 (CCPA 1971) and *In re Swinhart et al.*, 169 USPQ 226 (CCPA 1971).

With respect to claims 69 and 70, Zhang teaches the sample being a blood sample (Fig. 8A and col. 8, line 66-col. 9, line 13).

With respect to claim 71, Zhang et al. teach non-specific binding occurring on the first immunosensor (col. 28, line 40-col. 29, line 6).

4. Claims 7 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang (US 6,670,115) in view of Litman et al. (US 5,156,953), as applied to claim 1, further in view of Wescott et al. (US 2003/0207330).

Zhang in view of Litman et al. teach a second immobilized antibody specific to an antibody ligand, but fail to specifically teach the antibody ligand being a plasma protein.

Wescott et al. teach an immobilized antibody to a plasma protein of fibrinogen and a labeled plasma protein binding to the immobilized antibody (par. 202), in order to provide isolation of fibrinogen from a sample.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to use as the second immobilized protein the system of Zhang in view of Litman et al., an immobilized antibody to a plasma protein as taught by Wescott et al. because Litman et al. is generic with respect to the second immobilized antibody that can be incorporated onto the calibration surface and binds to a calibration ligand that is different from the measurement ligand and target analyte. One would be motivated to use the appropriate second immobilized antibody for detection of a desired calibration ligand. Regarding claim 10, although Wescott et al. do not specifically teach the binding affinity of the second antibody, the instant specification teaches that antibodies to analyte of \_ have an affinity constant within the recited range of about

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$1 \times 10^{-7}$ ) to about  $1 \times 10^{-15}$ ) at page 19, paragraph 85. As described above, Wescott et al. teach a labeled fibrinogen that binds to an immobilized antibody. Therefore according to the instant specification, the antibody to fibrinogen has an affinity within the recited range.

5. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang (US 6,670,115) in view of Litman et al. (US 5,156,953) as applied to claim 1, further in view of Pourmand et al. (US 2002/0155476).

Zhang in view of Litman et al. teach first and second immunosensor including first and second immobilized antibodies, respectively, but fail to teach the first and second immobilized antibodies immobilized on microparticles.

Pourmand et al. teach antibodies attached to an electrode through beads (par. 59, 70; antibodies, par. 54), in order to provide permanent attachment of molecules.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the immunosensor system of Zhang in view of Litman et al., antibodies immobilized to the electrode through beads as taught by Pourmand et al., in order to provide convenient and simple attachment of molecules to an electrode. Pourmand et al. do not specifically teach first and second immobilized antibodies immobilized on beads, however it would have been obvious to one having ordinary skill to attach the antibodies of Zhang on beads and attach them to the appropriate electrode. Furthermore Pourmand et al. do not teach the specific size of the beads. However, it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value for a

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result effective variable. “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation” Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). “No invention is involved in discovering optimum ranges of a process by routine experimentation.” Id. at 458, 105 USPQ at 236-237. The “discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art.” Since applicant has not disclosed that the specific limitations recited in instant claims 11 are for any particular purpose or solve any stated problem, and the prior art teaches that the size of beads having immobilized antibodies may be varied depending on the desired electrode size and desired number of antibodies to be immobilized to the substrate, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by the prior art by normal optimization procedures known in the microparticle art.

### ***Response to Arguments***

6. Applicant's arguments with respect to claims 1, 2, 5-7, 9-12 and 69-71 have been considered and are persuasive, but are moot in view of the new ground(s) of rejection. The previous rejections of the claims have been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Litman et al. teaching a first and second immunosensor, wherein the second immunosensor has an antibody that binds to an exogenous protein in the sample and is related to non-specific binding on the first immunosensor.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELANIE YU whose telephone number is (571)272-2933. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Melanie Yu/  
Patent Examiner, Art Unit 1641